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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/291,347	04/14/1999	JULIAN ALEXIS JOHN HANAK	CACO-0051	1979

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/291,347	HANAK ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 May 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *06 May 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): see attached.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *40-42*.

Claim(s) objected to: *44*.

Claim(s) rejected: *7-14,38, 39,43*.

Claim(s) withdrawn from consideration: *none*.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

ADVISORY ACTION

1. Claims 7-14, 38-44 are pending.

2. The request for entering amendments to claims 7-14, addition of claims 38-44, cancellation of claims 4-6, 15-18, 37, and arguments filed on 5/6/2003 under 37 CFR 1.116 in reply to the Final Action Paper No. 21 mailed on 12/2/2002 are acknowledged. The proposed amendments to the claims will be entered since they are deemed sufficient to overcome the 35 USC 103(a) rejections previously applied. Neither McMaster, Okorokov or Zhu teach a method for the production of RNA-free cellular components wherein the cellular component and the RNase are produced in the same cell. However, entry of these amendments is not deemed sufficient to place the application in condition for allowance for the following reasons.

3. Claim 14 would be rejected under 35 USC 112, second paragraph due to the recitation of "expression of said RNase is constitutive" since claim 14 depends upon claim 38, which is directed to a method wherein the expression of the RNase is inducible.

4. In regard to the rejections under 35 USC 112, first paragraph, Applicants argue that Okorokov and Zhu do not present any evidence that it would not be possible to prepare an RNA-free cellular component by inducing RNase expression in the cytoplasm. According to Applicants, Okorokov does not discuss the preparation of RNA-free cellular components as is claimed in the present application wherein the RNase expression is induced prior to isolating the cellular component. Applicants argue that if an inducible system is used, one can allow for the microbial cell to produce the cellular component and a later time induce the production of the RNase. Since neither Okorokov nor Zhu teach the preparation of RNA-free cellular components

wherein these components are made RNA-free by inducing the expression of RNase in the cytoplasm of the same cell, Applicants submit that these references do not show that the invention as claimed is not enabled. Applicants further argue that the application discloses several promoters which can be used in microbial cells and that the type of promoters that can be used under different conditions to get the required results in microbial cells are well known in the art. In addition, Applicants argue that the application discusses both specific and non-specific RNases and submit that a specific RNase such as T1 can cleave RNA into small pieces such that any cellular component being prepared would be RNA free. Applicants request that the Examiner provide a reference or an affidavit substantiating the position that RNAs would not be sufficiently degraded by an specific RNase. Furthermore, Applicants argue that there is no requirement that Applicants describe every RNase that could be used in the claimed invention. Therefore, it is Applicant's contention that the present invention is completely enabled.

5. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejections. The Examiner acknowledges that (1) neither Okorokov or Zhu teach the production of RNA-free cellular components wherein an RNase and the cellular component are made in the same cell, (2) an inducible system would allow one to express the RNase at a later time, after the cellular component has been made, (3) many microbial promoters are known in the art, and (4) many RNases are known in the art, however the Examiner disagrees with Applicant's contention that the claimed invention is enabled as it relates to expression of the RNase in the cytoplasm. It is noted that some of the claims are not limited to inducible systems, therefore arguments in regard to inducible systems are not applicable to claims wherein the expression system is constitutive. It is not the Examiner's contention that one of skill in the art

cannot design and construct an inducible expression system wherein the protein is expected to be expressed in the cytoplasm, if the polynucleotide encoding the protein is known. Furthermore, some of the claims are not limited to inducible systems. The enablement rejection, as discussed previously, was applied due to the evidence shown by Zhu et al. that while the recombinant expression of RNase I was intended to occur in the cytoplasm, 85% of the RNase activity was found in the periplasm and the remaining RNase found in the cytoplasm was most likely inactive. Furthermore, there is no experimental evidence presented by Applicants which show that one can obtain RNA-free cellular components by inducing the expression of an RNase in the cytoplasm as claimed. While one could argue that the claimed method can be practiced by first allowing the cellular components to be made and then, induce the expression of the RNase, the teachings of Zhu et al. indicate that the RNase produced may not be active in the cytoplasm. Therefore, in view of the teachings of the prior art and in the absence of experimental evidence, one of skill in the art cannot reasonably conclude that the claimed invention is enabled. As such, amended claims 7-14 and newly added claims 38-39, 43 would be rejected under 35 USC 112, first paragraph for the reasons of record and those set forth above.

6. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: 40-42

Claims(s) objected to: 44

Claim(s) rejected: 7-14, 38-39 and 43

Claim(s) withdrawn from consideration: NONE

7. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

8. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
May 26, 2003

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1800
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